

Entered Medline: 20030520

AB Mutations in the phosphotyrosine-binding domain protein ARH cause autosomal recessive hypercholesterolemia (ARH), an inherited form of hypercholesterolemia due to a tissue-specific defect in the removal of low density lipoproteins (LDL) from the circulation. LDL uptake by the LDL receptor (LDLR) is markedly reduced in the liver but is normal or only moderately impaired in cultured fibroblasts of ARH patients. To define the molecular mechanism underlying ARH we examined ARH mRNA and protein in fibroblasts and lymphocytes from six probands with different ARH mutations. None of the probands had detectable full-length ARH protein in fibroblasts or lymphoblasts. Five probands were homozygous for mutations that introduced premature termination codons. No relationship was apparent between the site of the mutation in ARH and the amount of mRNA. The only mutation identified in the remaining proband was a SINE VNTR Alu (SVA) retroposon insertion in intron 1, which was associated with no detectable ARH mRNA. (125) I-LDL degradation was normal in ARH fibroblasts, as previously reported. In contrast, LDLR function was markedly reduced in ARH lymphoblasts, despite a 2-fold increase in LDL cell surface binding in these cells. These data indicate that all ARH mutations characterized to date preclude the synthesis of full-length ARH and that ARH is required for normal LDLR function in lymphocytes and hepatocytes, but not in fibroblasts. Residual LDLR function in cells that do not require ARH may explain why ARH patients have lower plasma LDL levels than do patients with homozygous familial hypercholesterolemia who have no functional LDLRs.

L5 ANSWER 2 OF 6 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2001:670564 SCISEARCH

THE GENUINE ARTICLE: 462BQ

TITLE: DNA fingerprinting based on microsatellite-anchored fragment length polymorphisms, and isolation of sequence-specific PCR markers in lupin (*Lupinus angustifolius* L.)

AUTHOR: Yang H (Reprint); Sweetingham M W; Cowling W A; Smith P M C

CORPORATE SOURCE: Univ Western Australia, Ctr Legumes Mediterranean Agr, Nedlands, WA 6907, Australia (Reprint); Univ Western Australia, Dept Bot, Nedlands, WA 6907, Australia; Agr Western Australia, Bentley, WA 6983, Australia

COUNTRY OF AUTHOR: Australia

SOURCE: MOLECULAR BREEDING, (10 JUL 2001) Vol. 7, No. 3, pp. 203-209.

Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.

ISSN: 1380-3743.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 15

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We report a method of microsatellite-anchored fragment length polymorphisms for DNA fingerprinting. The method combines the concept of AFLP and the microsatellite-anchor primer technique. Genomic DNA was digested by one restriction enzyme *MseI*. One AFLP **adaptor** (*MseI adaptor*) was ligated onto the restriction fragments. DNA fingerprints were produced by PCR using one microsatellite-anchor primer in combination with one *MseI*-primer. The method allows co-amplification of over 100 DNA fragments containing microsatellite motifs per PCR. Polymorphisms detected from lupin by this method included those arising from variation in the number of microsatellite repeat units targeted by the microsatellite-anchor primers, from variation on the annealing sites for the SSR-anchor primers, from insertions/deletions outside the SSR region, and from variation in restriction sites. The first three types of polymorphisms were readily converted into sequence-specific PCR markers suitable for marker-assisted breeding.

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:334895 CAPLUS
DOCUMENT NUMBER: 136:32324
TITLE: Sequence-tagged microsatellite profiling (STMP): a rapid technique for developing SSR markers
AUTHOR(S): Hayden, M. J.; Sharp, P. J.
CORPORATE SOURCE: Plant Breeding Institute, University of Sydney, Camden, NSW 2570, Australia
SOURCE: Nucleic Acids Research (2001), 29(8), e43/1-e43/8
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe a technique, sequence-tagged microsatellite profiling (STMP), to rapidly generate large nos. of **simple sequence repeat** (SSR) markers from genomic or cDNA. This technique eliminates the need for library screening to identify SSR-containing clones and provides an .apprx.25-fold increase in sequencing throughput compared to traditional methods. STMP generates short but characteristic nucleotide sequence tags for fragments that are present within a pool of SSR amplicons. These tags are then ligated together to form concatemers for cloning and sequencing. The anal. of thousands of tags gives rise to a representational profile of the abundance and frequency of SSRs within the DNA pool, from which low copy sequences can be identified. As each tag contains sufficient nucleotide sequence for primer design, their conversion into PCR primers allows the amplification of corresponding full-length fragments from the pool of SSR amplicons. These fragments permit the full characterization of a SSR locus and provide flanking sequence for the development of a microsatellite marker. Alternatively, sequence tag primers can be used to directly amplify corresponding SSR loci from genomic DNA, thereby reducing the cost of developing a microsatellite marker to the synthesis of just one sequence-specific primer. We demonstrate the utility of STMP by the development of SSR markers in bread wheat.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 6 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1999-00837 BIOTECHDS
TITLE: Use of variable number tandem repeat allele and their flanking region; for genetic fingerprinting or other method of genotyping individual

AUTHOR: Firth G
PATENT ASSIGNEE: Firth G
LOCATION: Hitchin, UK.
PATENT INFO: WO 9842867 1 Oct 1998
APPLICATION INFO: WO 1998-GB840 20 Mar 1998
PRIORITY INFO: EP 1997-301917 21 Mar 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-609895 [51]
AN 1999-00837 BIOTECHDS

AB A method for the extraction of variable number tandem repeat polymorphism (**VNTR**) alleles is claimed and comprises making a mixture of **VNTR** alleles and their flanking regions from genomic DNA by: ligating an **adaptor** to genomic DNA fragments so that the 3' end of the **adaptor**-terminated fragment is blocked to prevent chain extension, and using these with **adaptor**-DNA primers and **VNTR** sense and antisense DNA to generate 3'- and 5'-flanking **VNTR** amplicers; and using the amplicers as DNA primers to extend on genomic DNA as the template and create the desired mixture of **VNTR** alleles and their flanking regions. Also claimed are: a method for treating a mixture of polymorphic alleles representative of a desired trait, by separating and re-annealing the DNA strands and

discarding mismatches; and a method for identifying an allele-linked to a trait by hybridizing a polymorphic allele representative of the trait with a mixture of non-trait alleles and selecting matches or mismatches to isolate the polymorphic trait-linked allele. The alleles generated can be used for genetic fingerprinting or obtaining selectable markers which segregate with specific traits. (101pp)

L5 ANSWER 5 OF 6 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1996-09957 BIOTECHDS
TITLE: Modified amplified fragment length polymorphism assay;
restriction fragment length polymorphism method for
detection of polymorphism, especially in microsatellite
DNA regions; DNA primer DNA sequence
AUTHOR: Morgante M; Vogel J M
PATENT ASSIGNEE: Du-Pont
LOCATION: Wilmington, DE, USA
PATENT INFO: WO 9617082 6 Jun 1996
APPLICATION INFO: WO 1995-US15150 21 Nov 1995
PRIORITY INFO: US 1994-346456 28 Nov 1994
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1996-277795 [28]
AN 1996-09957 BIOTECHDS
AB An improved method for detecting polymorphisms between 2 nucleic acid (NA) samples comprises amplifying segments of NA from each sample using primer-directed amplification and comparing the amplified fragments to detect differences. The improvement is that at least 1 of the primers used in the amplification consists of a perfect compound **simple sequence repeat** (SSR). Also claimed is a method comprising (a) digesting the NA with at least 1 restriction endonuclease to generate restriction fragments, (b) ligating **adaptor** segments to the ends of the fragments generated in (a), (c) amplifying the fragments of (b) using primer-directed amplification, where the amplification primers comprise a 1st primer consisting of a perfect compound SSR and a 2nd primer comprising a sequence complementary to an **adaptor** segment of (b), and (d) comparing the amplified NA products from each sample to detect the differences. The method represents a modified amplified fragment length polymorphism assay, and is particularly useful for genome fingerprinting, i.e. marking a genetic trait, and germplasm comparisons. (173pp)

=> d his

(FILE 'HOME' ENTERED AT 10:27:52 ON 02 JUN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 10:28:04 ON 02 JUN 2004

L1 141 S FIRTH G?/AU
L2 101 S VARIABLE NUMBER TANDEM REPEAT SEQUENCE OR VNTR SEQUENCE
L3 10974 S SIMPLE SEQUENCE REPEAT OR VNTR
L4 6 S ADAPTOR AND (L2 OR L3)
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)

=> s l1 and l3

L6 2 L1 AND L3

=> d ibib abs l6 1-2

L6 ANSWER 1 OF 2 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1999-00837 BIOTECHDS
TITLE: Use of variable number tandem repeat allele and their
flanking region;
for genetic fingerprinting or other method of genotyping
individual

AUTHOR: **Firth G**
 PATENT ASSIGNEE: Firth G
 LOCATION: Hitchin, UK.
 PATENT INFO: WO 9842867 1 Oct 1998
 APPLICATION INFO: WO 1998-GB840 20 Mar 1998
 PRIORITY INFO: EP 1997-301917 21 Mar 1997
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 OTHER SOURCE: WPI: 1998-609895 [51]

AN 1999-00837 BIOTECHDS

AB A method for the extraction of variable number tandem repeat polymorphism (**VNTR**) alleles is claimed and comprises making a mixture of **VNTR** alleles and their flanking regions from genomic DNA by: ligating an adaptor to genomic DNA fragments so that the 3' end of the adaptor-terminated fragment is blocked to prevent chain extension, and using these with adaptor-DNA primers and **VNTR** sense and antisense DNA to generate 3'- and 5'-flanking **VNTR** amplimers; and using the amplimers as DNA primers to extend on genomic DNA as the template and create the desired mixture of **VNTR** alleles and their flanking regions. Also claimed are: a method for treating a mixture of polymorphic alleles representative of a desired trait, by separating and re-annealing the DNA strands and discarding mismatches; and a method for identifying an allele-linked to a trait by hybridizing a polymorphic allele representative of the trait with a mixture of non-trait alleles and selecting matches or mismatches to isolate the polymorphic trait-linked allele. The alleles generated can be used for genetic fingerprinting or obtaining selectable markers which segregate with specific traits. (101pp)

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1998:672686 CAPLUS
 DOCUMENT NUMBER: 129:271497
 TITLE: Extraction of **VNTR** alleles and detection of polymorphic markers for inherited traits at multiple loci
 INVENTOR(S): **Firth, Greg**
 PATENT ASSIGNEE(S): UK
 SOURCE: PCT Int. Appl., 101 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9842867	A1	19981001	WO 1998-GB840	19980320
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9867376	A1	19981020	AU 1998-67376	19980320
AU 725963	B2	20001026		
GB 2338553	A1	19991222	GB 1999-22203	19980320
GB 2338553	B2	20010815		
EP 970246	A1	20000112	EP 1998-912592	19980320
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, FI				
JP 2001517086	T2	20011002	JP 1998-542088	19980320
NO 9904441	A	19991122	NO 1999-4441	19990913
US 2002058250	A1	20020516	US 2000-380932	20000118
PRIORITY APPLN. INFO.:			EP 1997-301917	A 19970321

WO 1998-GB840 A 19980320
EP 1998-42867 A 19980321

AB The invention presented is a novel method for the extraction of **VNTR** alleles and for the concomitant detection of polymorphic markers for inherited traits at multiple loci by simultaneous comparison of complex genomes from multiple individuals. The product is designated a Total Representation of Alleles that are Informative for a Trait (TRAIT). These alleles may be used directly as genetic markers or may be used as vehicles to facilitate precise localization of sequence variations responsible. Thus, a mixture of **VNTR** alleles and their flanks may be prepared by (1) dividing the genomic DNA of the species of interest into fragments; (2) ligating to each end of each fragment an adapter thereby forming a mixture of adapter-terminated fragments in which each 3'-end is blocked to prevent enzymic chain extension; (3) using a portion of the mixture of adapter-terminated fragments as templates with an adapter primer and a **VNTR** primer to create a mixture of 5'-flanking **VNTR** amplimers; (4) using a portion of the mixture of adapter-terminated fragments as templates with an adapter primer and a **VNTR** antisense primer to create a mixture of 3'-flanking **VNTR** amplimers; and (5) using genomic DNA of the one or more members of the species of interest as template with the mixture of 5'-flanking **VNTR** amplimers and the mixture of 3'-flanking **VNTR** amplimers as primers to make the desired mixture of **VNTR** alleles and their flanking regions. Using the synthesized **VNTR** alleles from different individuals or different sets of individuals, it is possible to select **VNTR** alleles common to all, or select **VNTR** alleles that are different. This is achieved by mixing the **VNTR** DNA, dissociation, and rehybridization followed by mis-match discrimination to identify and remove unwanted DNA. The technique was validated on a model system (genomic DNA from 43 dogs) designed to mimic a scenario of **VNTR** linkage disequil. that would be expected in the presence of a recessive trait.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 10:27:52 ON 02 JUN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 10:28:04 ON 02 JUN 2004

L1 141 S FIRTH G?/AU
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L3 10974 S SIMPLE SEQUENCE REPEAT OR VNTR
L4 6 S ADAPTOR AND (L2 OR L3)
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
L6 2 S L1 AND L3

=> s l3 and linker
L7 14 L3 AND LINKER

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 4 DUP REM L7 (10 DUPLICATES REMOVED)

=> d ibib abs 18 1-4

L8 ANSWER 1 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-09693 BIOTECHDS
TITLE: Detecting abnormal base-pairing in a nucleic acid duplex using mutant nucleic acid repair enzymes with attenuated catalytic activity, useful for diagnosing and prognosticating infection, diabetes, cancer or a metabolic disease; DNA duplex abnormal base repair detection for use in

disease diagnosis

AUTHOR: YUAN C; DATTA A
PATENT ASSIGNEE: YUAN C; DATTA A
PATENT INFO: US 2004014083 22 Jan 2004
APPLICATION INFO: US 2003-373238 24 Feb 2003
PRIORITY INFO: US 2003-373238 24 Feb 2003; US 2000-514016 25 Feb 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-121559 [12]
AN 2004-09693 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Detecting abnormal base-pairing in a nucleic acid duplex by contacting a nucleic acid duplex having or suspected of having an abnormal base-pairing with a mutant nucleic acid repair enzyme or its complex having binding affinity for the abnormal base-pairing in the duplex but with attenuated catalytic activity and detecting binding where the presence or quantity of the abnormal base-pairing in the duplex is assessed.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) detecting a mutation in a nucleic acid, comprising hybridizing a strand of a nucleic acid having or suspected of having a mutation with a complementary strand of a nucleic acid fragment having a wild type sequence; (2) detecting polymorphism in a gene locus, comprising hybridizing a target strand of a nucleic acid comprising a locus to be tested with a complementary reference strand of a nucleic acid comprising a known allele of the locus, whereby the allelic identity between the target and the reference strands results in the formation of a nucleic acid duplex without an abnormal base-pairing and the allelic difference between the target and the reference strands results in the formation of a nucleic acid duplex with an abnormal base-pairing, contacting the nucleic acid duplex formed with a mutant nucleic acid repair enzyme or its complex, wherein the mutant nucleic acid repair enzyme or its complex has binding affinity for the abnormal base-pairing in the duplex but has attenuated catalytic activity, and detecting binding between the nucleic acid duplex and the mutant nucleic acid repair enzyme or its complex, whereby the polymorphism in the locus is assessed; (3) purifying or separating nucleic acid duplex containing one or more abnormal base-pairing from a population of nucleic acid duplexes; (4) detecting and localizing an abnormal base-pairing in a nucleic acid duplex, comprising contacting a nucleic acid duplex having or suspected of having an abnormal base-pairing with a mutant nucleic acid repair enzyme or complex thereof, wherein the mutant nucleic acid repair enzyme or complex thereof has binding affinity for the abnormal base-pairing in the duplex but has attenuated catalytic activity; (5) a combination for detecting abnormal base-pairing in a nucleic acid duplex, comprising a mutant nucleic acid repair enzyme or complex thereof, and a reagent for detecting binding between abnormal base-pairing in a nucleic acid duplex and the mutant nucleic acid repair enzyme or complex thereof; (6) a kit comprising the combination of (5) and instructions for binding the mutant repair enzyme to nucleic acid duplexes to detect a mutation in a nucleic acid duplex, or to detect a polymorphism in a locus, or to diagnose a disease or disorder, or for gene mapping or identification by detecting polymorphisms or mutations; (7) an isolated substantially pure mutant nucleic acid repair enzyme that further comprises a detectable label, wherein the mutant enzyme has attenuated catalytic activity compared to the wild type but retains binding affinity for a nucleic acid duplex containing an abnormal base pairing; (8) an isolated substantially pure biotinylated mutant nucleic acid repair enzyme; (9) an article of manufacture comprising a packaging material, a mutant nucleic acid repair enzyme that has attenuated catalytic activity compared to the wild type but retains binding affinity for a nucleic acid duplex containing an abnormal base pairing, and a label indicating that the article is for use in detecting abnormal base-pairing in a nucleic acid duplex; (10) a combination for detecting and localizing an abnormal base-pairing in a nucleic acid duplex, comprising a mutant nucleic acid repair enzyme or

complex thereof, wherein the mutant enzyme that has attenuated catalytic activity compared to the wild type but retains binding affinity for a nucleic acid duplex containing an abnormal base pairing, and an exonuclease; (11) a kit comprising the combination of (10) and instructions for performing an assay for detecting and localizing an abnormal base-pairing in a nucleic acid duplex; (12) detecting polymorphism in a gene locus, comprising hybridizing a target strand of a nucleic acid comprising a locus to be tested with a complementary reference strand of a nucleic acid comprising a known allele of the locus, wherein the reference strand is so chosen that a first nucleic acid duplex formed between the reference strand and the target strand that contains an allele identical to the known allele in the reference strand; (13) a combination for detecting polymorphism in a gene locus, comprising a reference strand of a nucleic acid comprising a known allele of the locus complementary to a locus to be tested, wherein the reference strand is so chosen that a first nucleic acid duplex formed between the reference strand and the target strand that contains an allele identical to the known allele in the reference strand has a first binding affinity with a nucleic acid repair enzyme or complex thereof and a second nucleic acid duplex formed between the reference strand and the target strand that contains an allele different from the known allele in the reference strand has a second binding affinity with the nucleic acid repair enzyme or complex thereof, whereby the difference between the first and second binding affinities is detectable, a nucleic acid repair enzyme or complex thereof, and a reagent for detecting the difference between the first and second binding affinities is detectable; and (14) a kit comprising the combination of (13) and instructions for detecting the difference between the first and second binding affinities to detect a polymorphism in a locus, or to diagnose a disease or disorder, or for gene mapping or identification by detecting polymorphisms.

BIOTECHNOLOGY - Preferred Method: The nucleic acid duplex in detecting abnormal base-pairing is a DNA:DNA, a DNA:RNA or an RNA:RNA duplex, preferably a DNA:DNA duplex. The abnormal base-pairing is a base-pair mismatch, a base insertion, a base deletion or a pyrimidine dimer. The mutant nucleic acid repair enzyme or enzyme complex is selected from a mutant mutH, a mutant mutL, a mutant mutM, a mutant mutS, a mutant mutY, a mutant uvrD, a mutant dam, a mutant thymidine DNA glycosylase (TDG), a mutant mismatch-specific DNA glycosylase (MUG), a mutant AIkA, a mutant MLH1, a mutant MSH2, a mutant MSH3, a mutant MSH6, a mutant Exonuclease I, a mutant T4 endonuclease V, a mutant FEN1 (RAD27), a mutant DNA polymerase a, a mutant DNA polymerase a, a mutant RPA, a mutant PCNA, a mutant RFC, a mutant Exonuclease V, a mutant DNA polymerase III holoenzyme, a mutant DNA helicase, a mutant RecJ exonuclease and their combinations. The nucleic acid strand to be tested and the complementary wild-type nucleic acid strand in detecting a mutation are NA strands, wherein the mutation is associated with a disease or disorder, or infection by a pathological agent, and the method is used for prognosis or diagnosis of the presence or severity of the disease, disorder or infection. The polymorphism to be detected is a variable nucleotide type polymorphism (**VNTR**), or a single nucleotide polymorphism (SNP), wherein the SNP is a human genome SNP. The mutant nucleic acid repair enzyme or complex thereof is labeled with a detectable label or is labeled with biotin. The binding between the abnormal base-pairing and the biotin-labeled mutant nucleic acid repair enzyme or complex thereof is detected with a streptavidin labeled enzyme. The streptavidin labeled enzyme is peroxidase, a urease, an alkaline phosphatase, a luciferase or a glutathione S-transferase. The mutant nucleic acid repair enzyme or complex thereof is labeled with a detectable label. The nucleic acid duplex or the mutant nucleic acid repair enzyme or complex thereof is immobilized directly on the surface or is immobilized on the surface via a **linker**. The insoluble support is a silicon chip. The geometry of the support is selected from beads, pellets, disks, capillaries, hollow fibers, needles, solid fibers, random shapes, thin films, membranes and chips. The sample is a body fluid or a biological tissue, wherein the body fluid is urine, blood,

plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, mucus or amniotic fluid. The biological tissue is connective tissue, epithelium tissue, muscle tissue, nerve tissue, organs, tumors, lymph nodes, arteries or individual cells.

USE - The methods and compositions of the present invention are useful for the diagnosis and prognostication of infection, diabetes, cancer, an immune system disease or disorder, a metabolism disease, a muscle and bone disease or disorder, a nervous system disease or disorder, a signal disease, or a transporter disease (claimed).

EXAMPLE - No relevant example given. (108 pages)

L8 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002326173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12068981
TITLE: Predominant **VNTR** family of strains of
Mycobacterium tuberculosis isolated from South Asian
patients.
AUTHOR: Gascoyne-Binzi D M; Barlow R E L; Essex A; Gelletlie R;
Khan M A; Hafiz S; Collyns T A; Frizzell R; Hawkey P M
CORPORATE SOURCE: Department of Microbiology, The General Infirmary, Leeds,
UK.. deborahg@pathology.leeds.ac.uk
SOURCE: international journal of tuberculosis and lung disease :
official journal of the International Union against
Tuberculosis and Lung Disease, (2002 Jun) 6 (6) 492-6.
Journal code: 9706389. ISSN: 1027-3719.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020619
Last Updated on STN: 20021214
Entered Medline: 20021126

AB SETTING: Despite the low incidence of tuberculosis in the UK, some minority ethnic groups, particularly those originating from South Asia, experience very high incidence rates. OBJECTIVE: Comparison of the variable number tandem repeat (**VNTR**) profiles of strains of Mycobacterium tuberculosis circulating in an immigrant community in the UK with those found in the country of ethnic origin. DESIGN: Isolates of M. tuberculosis were collected from samples obtained from patients attending clinics in Leeds and Bradford, UK and Rawalpindi, Pakistan. Strains were compared using **VNTR** analysis and mixed-linker PCR.

RESULTS: Comparison of **VNTR** profiles found that one profile (42235) represented 37% of patient isolates from Rawalpindi and 23% of patient isolates in Leeds and Bradford, where it was associated exclusively with patients with South Asian names. A second profile (02235) represented 15% of patient isolates in Leeds and Bradford, and was also exclusively associated with the South Asian community. These profiles could be subdivided by mixed-linker PCR analysis.

CONCLUSION: The **VNTR** profile 42235 may represent a family of strains commonly found in communities associated with South Asia.

L8 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999335545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10405410
TITLE: Comparison of methods based on different molecular epidemiological markers for typing of Mycobacterium tuberculosis complex strains: interlaboratory study of discriminatory power and reproducibility.
AUTHOR: Kremer K; van Soolingen D; Frothingham R; Haas W H; Hermans P W; Martin C; Palittapongarnpim P; Plikaytis B B; Riley L W; Yakerus M A; Musser J M; van Embden J D
CORPORATE SOURCE: Diagnostic Laboratory for Infectious Diseases and Perinatal Screening, National Institute of Public Health and the Environment, 3720 BA Bilthoven, The Netherlands..

kristin.kremer@rivm.nl
CONTRACT NUMBER: AI-370040 (NIAID)
DA-09238 (NIDA)
SOURCE: Journal of clinical microbiology, (1999 Aug) 37 (8)
2607-18.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812

AB In this study, the currently known typing methods for *Mycobacterium tuberculosis* isolates were evaluated with regard to reproducibility, discrimination, and specificity. Therefore, 90 *M. tuberculosis* complex strains, originating from 38 countries, were tested in five restriction fragment length polymorphism (RFLP) typing methods and in seven PCR-based assays. In all methods, one or more repetitive DNA elements were targeted. The strain typing and the DNA fingerprint analysis were performed in the laboratory most experienced in the respective method. To examine intralaboratory reproducibility, blinded duplicate samples were included. The specificities of the various methods were tested by inclusion of 10 non-*M. tuberculosis* complex strains. All five RFLP typing methods were highly reproducible. The reliability of the PCR-based methods was highest for the mixed-linker PCR, followed by variable numbers of tandem repeat (VNTR) typing and spoligotyping. In contrast, the double repetitive element PCR (DRE-PCR), IS6110 inverse PCR, IS6110 ampliprinting, and arbitrarily primed PCR (APPCR) typing were found to be poorly reproducible. The 90 strains were best discriminated by IS6110 RFLP typing, yielding 84 different banding patterns, followed by mixed-linker PCR (81 patterns), APPCR (71 patterns), RFLP using the polymorphic GC-rich sequence as a probe (70 patterns), DRE-PCR (63 patterns), spoligotyping (61 patterns), and VNTR typing (56 patterns). We conclude that for epidemiological investigations, strain differentiation by IS6110 RFLP or mixed-linker PCR are the methods of choice. A strong association was found between the results of different genetic markers, indicating a clonal population structure of *M. tuberculosis* strains. Several separate genotype families within the *M. tuberculosis* complex could be recognized on the basis of the genetic markers used.

L8 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 88084442 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3692173
TITLE: Structure and in vitro transcription of a mouse B1 cluster containing a unique B1 dimer.
AUTHOR: Moshier J A; Deutch A H; Huang R C
CORPORATE SOURCE: Department of Biology, Johns Hopkins University, Baltimore, MD 21218.
CONTRACT NUMBER: 1P01AG03663 (NIA)
R01AG04350 (NIA)
SOURCE: Gene, (1987) 58 (1) 19-27.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M18260
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19880210

AB A highly repetitive DNA element located 950 bp upstream from a mouse U2

small nuclear RNA gene has been cloned and characterized. The repetitive element is composed of a **simple sequence** **repeat** and a cluster of three B1 sequences. Two of these B1 elements are arranged head-to-tail and are joined by an oligo(dA)-rich **linker**. This unique B1 dimer, comprised of 339 bp, resembles the dimeric structure of primate Alu-family sequences, particularly that of a prototypic human Alu element. The other B1 element within the mouse cluster is a typical monomeric unit. Transcription studies performed in HeLa cell extracts with deletion mutants of the B1 cluster reveal that the single B1 unit is expressed at least 50 times more efficiently than the B1 dimer region. Furthermore, the B1 dimer which contains mutations in the first polymerase III promoter region is not transcribed end-to-end. We conclude that this B1 dimer is unlikely to give rise to a new dimeric retroposon family in the mouse genome.

=> d his

(FILE 'HOME' ENTERED AT 10:27:52 ON 02 JUN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 10:28:04 ON 02 JUN 2004

L1 141 S FIRTH G?/AU
L2 101 S VARIABLE NUMBER TANDEM REPEAT SEQUENCE OR VNTR SEQUENCE
L3 10974 S SIMPLE SEQUENCE REPEAT OR VNTR
L4 6 S ADAPTOR AND (L2 OR L3)
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
L6 2 S L1 AND L3
L7 14 S L3 AND LINKER
L8 4 DUP REM L7 (10 DUPLICATES REMOVED)

=> s (l3 or l2) and (mixture or plurality or set)
L9 717 (L3 OR L2) AND (MIXTURE OR PLURALITY OR SET)

=> s l9 and tag
L10 10 L9 AND TAG

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 5 DUP REM L10 (5 DUPLICATES REMOVED)

=> d ibib abs l11 1-5

L11 ANSWER 1 OF 5 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 1
ACCESSION NUMBER: 2003:1099247 SCISEARCH
THE GENUINE ARTICLE: 752DM
TITLE: Transferable EST-SSR markers for the study of polymorphism
and genetic diversity in bread wheat
AUTHOR: Gupta P K (Reprint); Rustgi S; Sharma S; Singh R; Kumar N;
Balyan H S
CORPORATE SOURCE: Ch Charan Singh Univ, Dept Agr Bot, Mol Biol Lab, Meerut
250004, Uttar Pradesh, India (Reprint)
COUNTRY OF AUTHOR: India
SOURCE: MOLECULAR GENETICS AND GENOMICS, (DEC 2003) Vol. 270, No.
4, pp. 315-323.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY
10010 USA.
ISSN: 1617-4615.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND TALL FORMATS

AB Nearly 900 SSRs (simple sequence repeats) were identified among 15,000
ESTs (expressed sequence tags) belonging to bread wheat (*Triticum*
aestivum L.). The SSRs were defined by their minimum length, which ranged

from 14 to 21 bp. The maximum length ranged from 24 to 87 bp depending upon the length of the repeat unit itself (1-7 bp). The average density of SSRs was one SSR per 9.2 kb of EST sequence screened. The trinucleotide repeats were the most abundant SSRs detected. As a representative sample, 78 primer pairs were designed, which were also used to screen the dbEST entries for *Hordeum vulgare* and *Triticum tauschii* (donor of the D-genome of cultivated wheat) using a cut-off E (expectation) value of 0.01. On the basis of in silico analysis, up to 55.12% of the primer pairs exhibited transferability from *Triticum* to *Hordeum*, indicating that the sequences flanking the SSRs are not only conserved within a single genus but also between related genera in Poaceae. Primer pairs for the 78 SSRs were synthesized and used successfully for the study of (1) their transferability to 18 related wild species and five cereal species (barley, oat, rye, rice and maize); and (2) polymorphism between the parents of four mapping populations available with us. A subset of 20 EST-SSR primers was also used to assess genetic diversity in a collection of 52 elite exotic wheat genotypes. This was done with a view to compare their utility relative to other molecular markers (gSSRs, AFLPs, and SAMPL) previously used by us for the same purpose with the same set of 52 bread wheat genotypes. Although only a low level of polymorphism was detected, relative to that observed with genomic SSRs, the study suggested that EST-SSRs can be successfully used for a variety of purposes, and may actually prove superior to SSR markers extracted from genomic libraries for diversity estimation and transferability.

L11 ANSWER 2 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2002239980 EMBASE
TITLE: Generation and comparison of EST-derived SSRs and SNPs in barley (*Hordeum vulgare* L.).
AUTHOR: Kota R.; Varshney R.K.; Thiel T.; Dehmer K.J.; Graner A.
CORPORATE SOURCE: R. Kota, Inst. Plant Genet./Crop Plant Res., Correnstr. 3, 06466 Gatersleben, Germany. kota@ipk-gatersleben.de
SOURCE: Hereditas, (2002) 135/2-3 (145-151).
Refs: 31
ISSN: 0018-0661 CODEN: HEREAY
COUNTRY: Sweden
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The progress of genome sequencing projects of model plants like barley, combined with the recent advances of high throughput assays, has provided a wealth of sequence information. This information is being employed to develop a high density transcript map of barley (*Hordeum vulgare* L.). To achieve this goal, the available EST database is being used as a resource for the development of novel microsatellite (SSR) and single nucleotide polymorphism (SNP) markers. So far, a total of 692 microsatellites representing different di-, tri- and tetra-nucleotide repeats were identified from a set of 19,000 EST sequences. Non-redundant SSRs have been used for mapping and so far 76 microsatellite loci were mapped. In addition to the 180 SNP primer pairs, which were designed to target specific ESTs, 72 were polymorphic among the seven genotypes examined here. Of these, 60 SNPs have been mapped applying a denaturing HPLC approach. To examine the potential of the EST-derived markers for pedigree studies, EST-derived SSRs (75 loci) and SNPs (72 loci) were used to fingerprint a set of seven genotypes. The results show that although both marker types yielded similar groupings, a larger data set of both SSRs and SNPs is necessary to obtain stable clusters in unrelated germplasm.

L11 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
ACCESSION NUMBER: 2001:172999 BIOSIS
DOCUMENT NUMBER: PREV200100172999

TITLE: Development and characterisation of **simple sequence repeat** (SSR) markers for white clover (*Trifolium repens* L.).
AUTHOR(S): Kolliker, R.; Jones, E. S.; Drayton, M. C.; Dupal, M. P.; Forster, J. W. [Reprint author]
CORPORATE SOURCE: Plant Biotechnology Centre, Agriculture Victoria, La Trobe University, Bundoora, VIC, 3083, Australia
john.forster@nre.vic.gov.au
SOURCE: Theoretical and Applied Genetics, (February, 2001) Vol. 102, No. 2-3, pp. 416-424. print.
CODEN: THAGA6. ISSN: 0040-5752.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Apr 2001

Last Updated on STN: 18 Feb 2002

AB Highly informative molecular markers, such as simple sequence repeats (SSRs), can greatly accelerate breeding programs. The aim of this study was to develop and characterise a comprehensive **set** of SSR markers for white clover (*Trifolium repens* L.), which can be used to **tag** genes and quantitative trait loci controlling traits of agronomic interest. Sequence analysis of 1123 clones from genomic libraries enriched for (CA)_n repeats yielded 793 clones containing SSR loci. The majority of SSRs consisted of perfect dinucleotide repeats, only 7% being trinucleotide repeats. After exclusion of redundant sequences and SSR loci with less than 25 bp of flanking sequence, 397 potentially useful SSRs remained. Primer pairs were designed for 117 SSR loci and PCR products in the expected size range were amplified from 101 loci. These markers were highly polymorphic, 88% detecting polymorphism across seven white clover genotypes with an average allele number of 4.8. Four primer pairs were tested in an F2 population revealing Mendelian segregation. Successful cross-species amplification was achieved in at least one out of eight legume species for 46 of 54 primer pairs. The rate of successful amplification was significantly higher for *Trifolium* species when compared to species of other genera. The markers developed in this study not only provide valuable tools for molecular breeding of white clover but may also have applications in related taxa.

L11 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:652123 CAPLUS

DOCUMENT NUMBER: 137:227408

TITLE: Generation and comparison of EST-derived SSRs and SNPs in barley (*Hordeum vulgare* L.)

AUTHOR(S): Kota, Raja; Varshney, Rajeev Kumar; Thiel, Thomas; Dehmer, Klaus Johannes; Graner, Andreas

CORPORATE SOURCE: Institute of Plant Genetics and Crop Plant Research, Gatersleben, Germany

SOURCE: *Hereditas* (Lund, Sweden) (2001), 135(2-3), 145-151
CODEN: HEREAY; ISSN: 0018-0661

PUBLISHER: Mendelian Society of Lund

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The progress of genome sequencing projects of model plants like barley, combined with the recent advances of high throughput assays, has provided a wealth of sequence information. This information is being employed to develop a high d. transcript map of barley (*Hordeum vulgare*). To achieve this goal, the available EST database is being used as a resource for the development of novel microsatellite (SSR) and single nucleotide polymorphism (SNP) markers. So far, a total of 692 microsatellites representing different di-, tri- and tetra-nucleotide repeats were identified from a **set** of 19,000 EST sequences. Non-redundant SSRs have been used for mapping and so far 76 microsatellite loci were mapped. In addition to the 180 SNP primer pairs, which were designed to target specific ESTs, 72 were polymorphic among the 7 genotypes examined. Of these, 60 SNPs were mapped applying a denaturing HPLC approach. To examine the potential of the EST-derived markers for pedigree studies,

EST-derived SSRs (75 loci) and SNPs (72 loci) were used to fingerprint a set of 7 genotypes. The results show that although both marker types yielded similar groupings, a larger data set of both SSRs and SNPs is necessary to obtain stable clusters in unrelated germplasm.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
ACCESSION NUMBER: 2001:151463 BIOSIS
DOCUMENT NUMBER: PREV200100151463
TITLE: Identification and mapping of QTLs conferring resistance to ascochyta blight in chickpea.
AUTHOR(S): Santra, Dipak K.; Tekeoglu, Mucella; Ratnaparkhe, MiLind;
Kaiser, Walter J.; Muehlbauer, Fred J. [Reprint author]
CORPORATE SOURCE: USDA-ARS, Washington State Univ., 303 Johnson Hall,
Pullman, WA, 99164-6434, USA
muehlbau@wsu.edu
SOURCE: Crop Science, (November-December, 2000) Vol. 40, No. 6, pp.
1606-1612. print.
CODEN: CRPSAY. ISSN: 0011-183X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2001
Last Updated on STN: 15 Feb 2002

AB Ascochyta blight, caused by Ascochyta rabiei (Pass.) Laboratory, is a devastating disease of chickpea (*Cicer arietinum* L.) worldwide. Resistant germplasm has been identified and the genetics of resistance has been the subject of numerous studies. The objectives of the present study were to determine the genetics of resistance to ascochyta blight of chickpea and to map and tag the chromosomal regions involved using molecular markers. We used a set of 142 F5:6 recombinant inbred lines (RILs) obtained from an interspecific cross of *C. arietinum* (FLIP84-92C, resistant parent) X *C. reticulatum* Lad. (PI 599072, susceptible parent). The RILs were scored for disease reactions in the field over 2 yr and were genotyped for polymorphic molecular markers (isozyme, random amplified polymorphic DNA (RAPD), and inter simple sequence repeat (ISSR)) in the laboratory. The disease was scored quantitatively and data were used for QTL analysis. A linkage map was established that comprised nine linkage groups containing 116 markers covering a map distance of 981.6 centimorgans (cM) with an average distance of 8.4 cM between markers. Two quantitative trait loci (QTLs), QTL-1 and QTL-2, conferring resistance to ascochyta blight, were identified which accounted for 50.3 and 45.0% of the estimated phenotypic variation in 1997 and 1998, respectively, and were mapped to linkage groups 6 and 1, respectively. Two RAPD markers flanked QTL-1 and were 10.9 cM apart while one ISSR marker and an isozyme marker flanked QTL-2 and were 5.9 cM apart. These markers can be used for marker-assisted selection for ascochyta blight resistance in chickpea breeding programs, and to develop durable resistant cultivars through gene pyramiding.

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FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 10:28:04 ON 02 JUN 2004

L1 141 S FIRTH G?/AU
L2 101 S VARIABLE NUMBER TANDEM REPEAT SEQUENCE OR VNTR SEQUENCE
L3 10974 S SIMPLE SEQUENCE REPEAT OR VNTR
L4 6 S ADAPTOR AND (L2 OR L3)
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
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L8 4 DUP REM L7 (10 DUPLICATES REMOVED)
L9 717 S (L3 OR L2) AND (MIXTURE OR PLURALITY OR SET)
L10 10 S L9 AND TAG
L11 5 DUP REM L10 (5 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:Y

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changes
NEWS 6 MAR 03 MEDLINE and LMEDLINE reloaded
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NEWS 11 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12 APR 26 PROMT: New display field available
NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field
available
NEWS 14 APR 26 LITALERT now available on STN
NEWS 15 APR 27 NLDB: New search and display fields available
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NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May
and June 2004
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